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Fibroblastic polyp of the colon: clinicopathological analysis of 10 cases with emphasis on its common association with serrated crypts

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Aims: To describe the clinical and pathological features of 10 further cases of fibroblastic polyps (FP), a recently described, distinctive type of colorectal mucosal polyp.
Methods and results: The patients were seven women and three men with ages ranging from 44 to 63 years. The lesions ranged in size from 2 to 4 mm. Eight of the polyps were located in the sigmoid colon. Five cases were associated with hyperplastic polyps. Histologically, FP displayed bland, plump spindle cells with oval nuclei arranged as bundles parallel to the surface or as haphazardly orientated sheets with a focal periglandular or perivascular concentric arrangement. Eight polyps represented mixed fibroblastic/hyperplastic polyps as they contained serrated (hyperplastic) crypts. Immunohistochemically, all cases were positive for vimentin and negative for desmin, smooth-muscle actin, h-caldesmon, S100 protein, c-Kit, epithelial membrane antigen, cytokeratin AE1/3, CD34, CD68, COX-2, and factor XIIIa. Ultrastructural examination supported the fibroblastic nature of the tumour cells.
Conclusions: FP is a distinctive type of benign mucosal colorectal polyp characterized by its distal location, small size, frequent association with hyperplastic polyps, distinct morphological appearance and typical immunonegativity for markers of specific differentiation. FP with serrated crypts (mixed fibroblastic/hyperplastic polyp) represents a frequent variant of this lesion. Pathologists should recognize FP and discriminate it from other types of colorectal polyps.

Keywords: colonic polyps, fibroblastic polyps, hyperplastic polyps

Abbreviations: FP, fibroblastic polyp(s); IFP, inflammatory fibroid polyp

Introduction

Fibroblastic polyp (FP) was recently described by Eslami-Varzaneh *et al.*[1] as a distinctive type of mesenchymal polyp of the colorectum characterized by a mucosal proliferation of monomorphic spindle cells leading to a wide separation and disorganization of the colonic crypts. In their series of 14 cases, FP occurred almost exclusively in the left and distal colon and all but one lesion measured less than 10 mm in diameter. In addition to the original description, FP has been reported only in a small series of four cases published as a 'letter to the editor'.[2] A notable finding, observed in three cases from the original series and in two of the cases reported by Zamecnik and Chlumska, was the presence of hyperplastic polyps admixed with or immediately adjacent to FP.[1,2] Immunohistochemically, vimentin was strongly positive in all 14 FP of Eslami-Varzaneh *et al.*,[1] whereas all four cases of Zamecnik and Chlumska[2]

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reacted to fascin, a putative marker of follicular dendritic cells. Ultrastructural analysis supported a fibroblastic phenotype for the tumour cells.[1]

We have collected a series of 10 FP, including eight mixed fibroblastic/hyperplastic polyps. Herein, we present their clinical, histological, immunohistochemical and ultrastructural features. Our aim was to expand on the morphological spectrum of this lesion, which is not well known to pathologists, and to emphasize its common association with serrated crypts.

Materials and methods

Eight cases were retrieved from the archival files of the Pathology Department at the Hillel Yaffe Medical Centre. Two additional cases were contributed by one of the authors (H.D.A.).

All specimens were fixed in formalin and embedded in paraffin. Clinical data, endoscopic details and haematoxylin and eosin-stained sections were reviewed. Additional sections from six cases were stained with the Masson's trichrome method for collagen fibres. For electron microscopy, representative tissue was retrieved from paraffin-embedded blocks in two cases.

IMMUNOHISTOCHEMISTRY

Sections (4 μm) from eight of the cases were cut from the paraffin blocks and mounted on charged slides. The sections were deparaffinized, rehydrated and treated with 1% hydrogen peroxide for 10 min to block endogenous peroxidase activity. Staining was performed after microwave antigen retrieval. The antibodies used in the study together with their sources and dilutions are shown in Table 1. Immunostaining using the avidin–biotin complex and peroxidase methods and diaminobenzidine as the chromogen was performed using a Ventana BenchMark Immunostainer™ (Ventana Medical Systems, Tucson, AZ, USA). Appropriate positive and negative controls were used for each antibody.

Results

CLINICAL FINDINGS

The notable clinical features of the 10 cases are summarized in Table 2.

The median age of the patients was 59 years (range 44–63 years). Seven of them were females and three were males. In nine of the patients the polyp was encountered during screening colonoscopy for colorectal carcinoma. The remaining patient (case 4), who also had a tubular adenoma, had a history of mild rectal bleeding. All FP measured between 2 and 4 mm in greatest dimension. Eight were located in the sigmoid, one in the descending colon and one in the ascending colon. Associated hyperplastic and adeno-

Table 1. List of antibodies used with sources and dilutions

	Antibody	Source	Dilution
1	Vimentin	Zymed, South San Francisco, CA, USA	Ready to use
2	Smooth-muscle actin	Zymed	Ready to use
3	Cytokeratin AE1/3	Zymed	Ready to use
4	Ki67	Zymed	Ready to use
5	Desmin	Biogenex, San Ramon, CA, USA	Ready to use
6	Factor XIIIa	Biogenex	Ready to use
7	S100 protein	Dako, Carpinteria, CA, USA	Ready to use
8	Epithelial membrane antigen	Dako	Ready to use
9	PG-M1 (CD68)	Dako	Ready to use
10	COX-2	Dako	1 : 140
11	h-caldesmon	Novocastra, Newcastle, UK	1 : 25
12	c-Kit (CD117)	Novocastra	1 : 400
13	CD34	Signet, Dedham, CA, USA	Ready to use

Table 2. Clinical features of fibroblastic polyps

Case	Gender	Age (years)	Site	Size (mm)	Associated colonic lesions
1	F	46	DC	3	None
2	F	62	Sigmoid	4	None
3	M	44	Sigmoid	2	HP
4	M	53	Sigmoid	2	TA
5	F	59	AC	3	HP
6	F	59	Sigmoid	3	None
7	F	63	Sigmoid	3	HP and TA
8	F	47	Sigmoid	3	HP
9	M	63	Sigmoid	4	None
10	F	62	Sigmoid	3	HP, multiple

F, Female; M, male; DC, descending colon; AC, ascending colon; HP, hyperplastic polyp; TA, tubular adenoma.

matous polyps were observed in five and two cases, respectively, including one case with both types of lesions. All patients remained asymptomatic after follow-up of between 4 months and 3 years (mean 18 months). Follow-up colonoscopy performed in five of the patients yielded no pathological changes.

PATHOLOGICAL FINDINGS

Microscopic findings

All polyps were characterized by the presence of uniform, bland, plump spindle cells in the lamina propria that surrounded and separated the colonic crypts (Figure 1). The cells displayed abundant pale eosinophilic cytoplasm with indistinct cell borders and oval to fusiform nuclei (Figure 2). The cytomorphology, especially in the context of the histochemical, immunohistochemical and ultrastructural findings (see below), was fully compatible with a fibroblastic lesion. None of the polyps displayed pleomorphism, necrosis or mitotic activity. A few scattered inflammatory cells, mainly comprising eosinophils, were seen in most cases. Masson's trichrome stain revealed thin, delicate collagen fibres separating the fibroblastic cells (Figure 3).

Eight (80%) of the polyps were of mixed fibroblastic/hyperplastic type. This variant was characterized by the micropapillary architecture of the surface epithelium and by the intimate admixture of the fibroblastic cells with crypts exhibiting intraluminal epithelial infoldings, creating a serrated or star-shaped configuration (Figures 1 and 4).

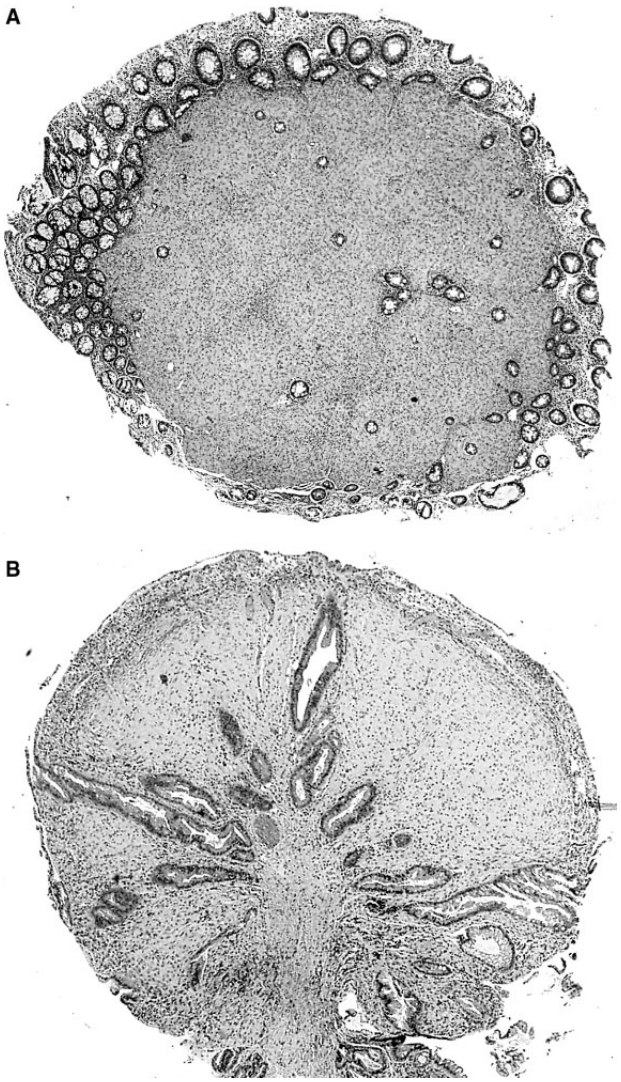

Figure 1. A, Low-power view of fibroblastic polyp of the colon without serrated glands. **B,** Low-power view of fibroblastic polyp of the colon with serrated glands.

A vague zoning phenomenon was apparent in five polyps, with superficial bundles of spindle cells arranged parallel to the surface changing to deeper, haphazardly orientated sheets of plump cells with a focal pericryptal and perivascular concentric arrangement (Figures 2 and 5). In seven cases there was a thin zone of uninvolved, mildly inflamed lamina propria separating the fibroblastic cells from the superficial lining which was eroded in two polyps (Figure 5). The muscularis mucosae, present in six of the cases, displayed mild disorganization with occasional thin bundles extending radially toward the surface. The

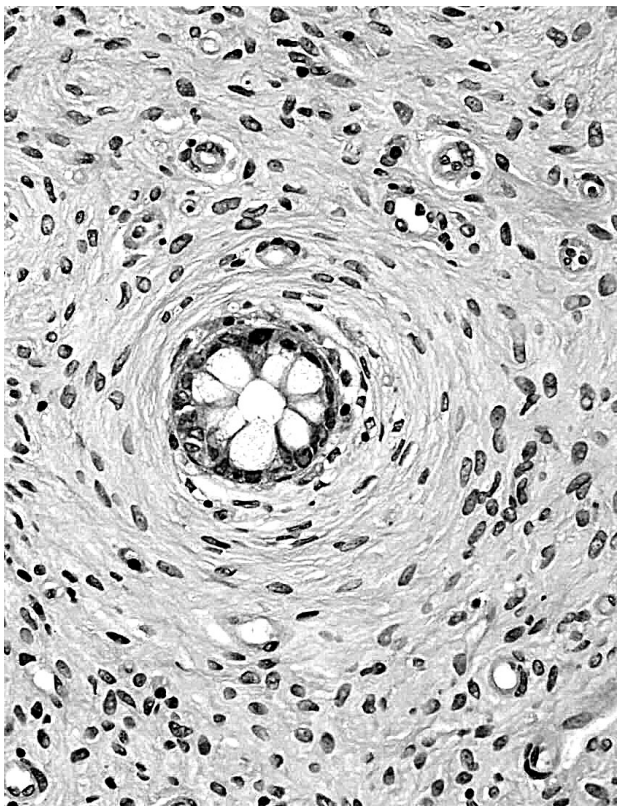

Figure 2. Higher power view of fibroblastic polyp displaying cells with abundant eosinophilic cytoplasm, indistinct cell borders and oval nuclei. Note the concentric pericryptal arrangement.

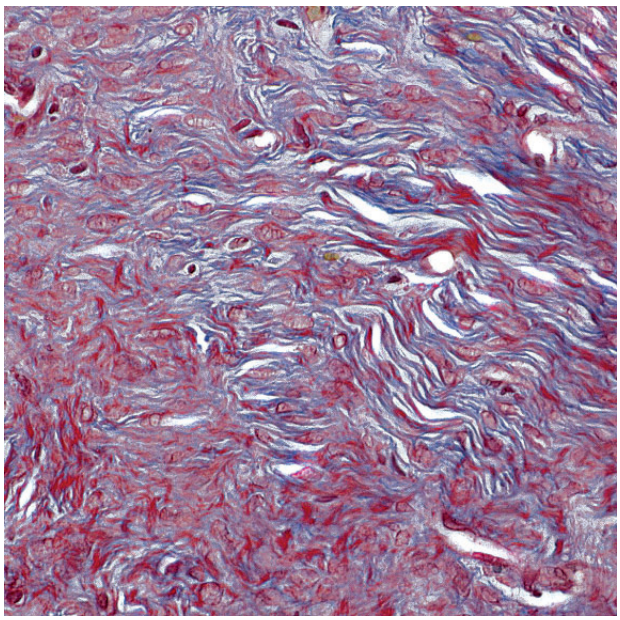

Figure 3. Masson's trichrome stain showing fine fibrillary collagen among the fibroblastic cells.

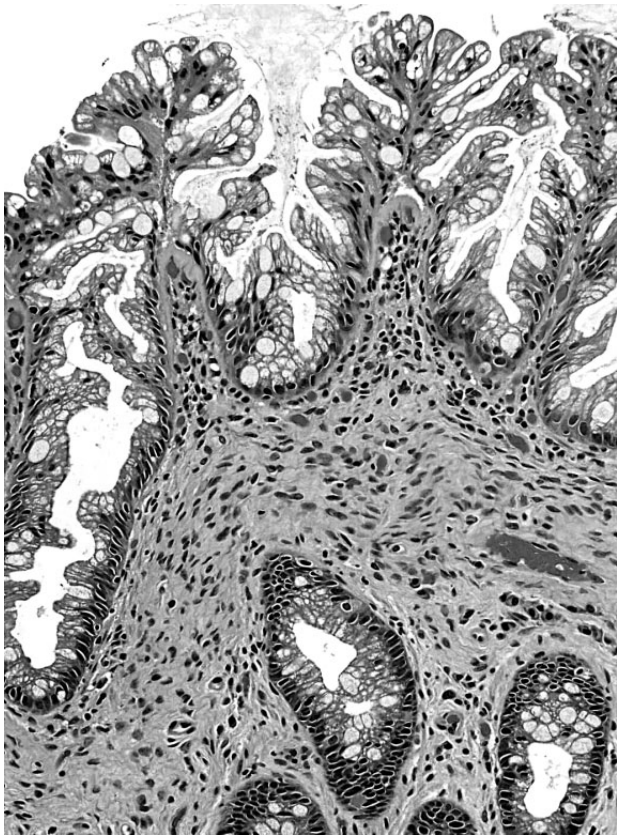

Figure 4. Mixed fibroblastic/fibroblastic polyp (fibroblastic polyp with serrated crypts).

superficial submucosa was included in only two lesions and was not involved by the fibroblastic cells. A remarkable histological finding seen in the periphery of one of the polyps (case 3) was the presence of small, well-demarcated whorls of plump spindle cells morphologically resembling meningothelial-like nodules (Figure 6).

Immunohistochemical and ultrastructural findings

All cases were strongly and diffusely immunoreactive for vimentin (Figure 7) and negative for smooth-muscle actin, desmin, h-caldesmon, S100 protein, c-Kit, epithelial membrane antigen, cytokeratin AE1/3, CD34, PG-M1, COX-2, and factor XIIIa. Ki67 revealed a low proliferation index of approximately 1%.

Ultrastructural examination disclosed flattened cells with slender, long cytoplasmic processes closely associated with collagen fibrils of normal periodicity (Figure 8). The cells had rough endoplasmic reticulum and intermediate filaments and lacked basal lamina, focal densities or subplasmalemmal densities. These findings were in accordance with a fibroblastic phenotype.

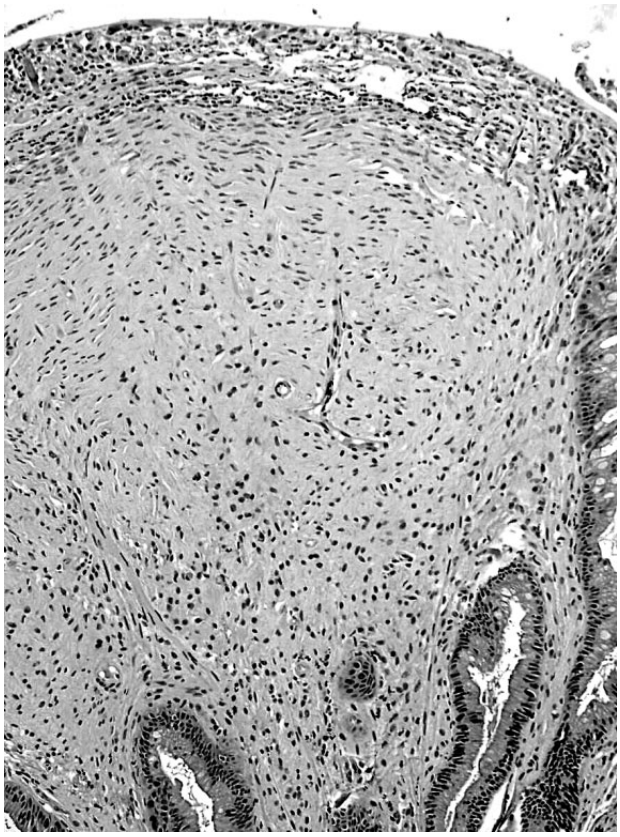

Figure 5. Fibroblastic polyp showing zonation with superficial bundles of spindle cells arranged parallel to the surface and deeper haphazardly orientated sheets of plump cells. Note the intervening thin zone of inflamed lamina propria between the lesion and the eroded surface.

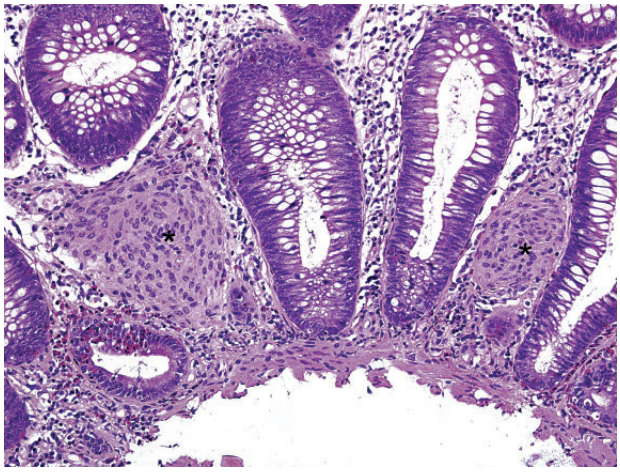

Figure 6. Section from the periphery of a fibroblastic polyp (case 3) showing two small, well-demarcated whorls of spindle and plump cells morphologically resembling meningothelial-like nodules (asterisks).

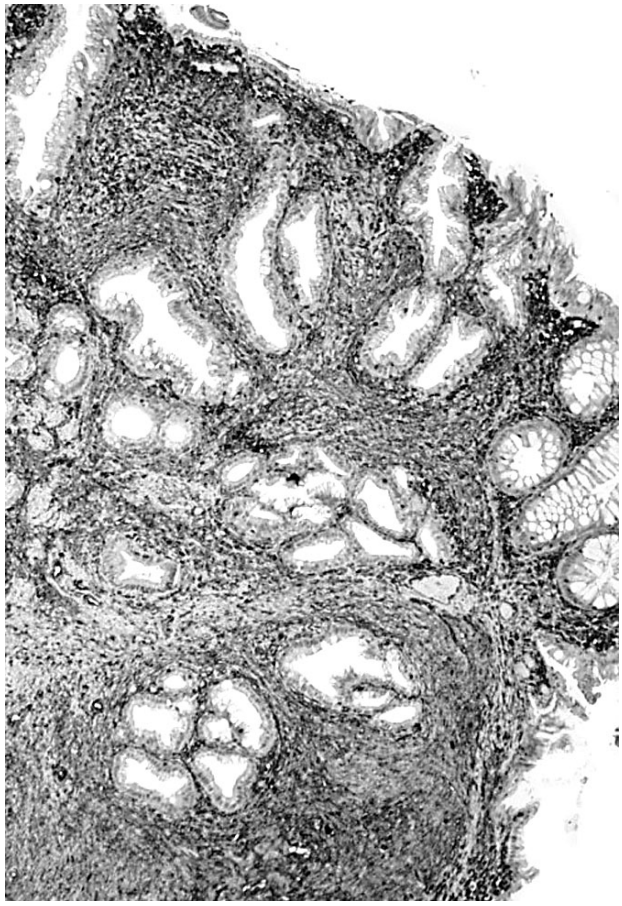

Figure 7. Vimentin is strongly and diffusely immunopositive in a fibroblastic polyp.

Discussion

This study validates previous findings on FP and confirms that this lesion represents a site-specific colorectal lesion with characteristic clinical and pathological features.[1] Including the present 10 cases, there is a total of 28 FP reported in the literature.[1,2] The age range of all patients was 37–84 (mean 60 years, median 59 years) with a moderate female predominance (65% of the cases). Only three of 28 patients were symptomatic: one from this series had mild rectal bleeding and in two previous cases the clinical diagnoses were dyspepsia and colitis.[2] All reported FP were solitary lesions and endoscopically described as polyps. Twenty-five cases measured between 2 and 5 mm. Three additional cases from the Eslami-Varzaneh *et al.*[1] series measured 7, 8 and 15 mm, respectively. Twenty-three (82%) polyps were located in the rectosigmoid colon, two in the ascending colon, two in the descending colon and one in the splenic flexure. Five of our cases (50%) and nine of 18 (50%) previous

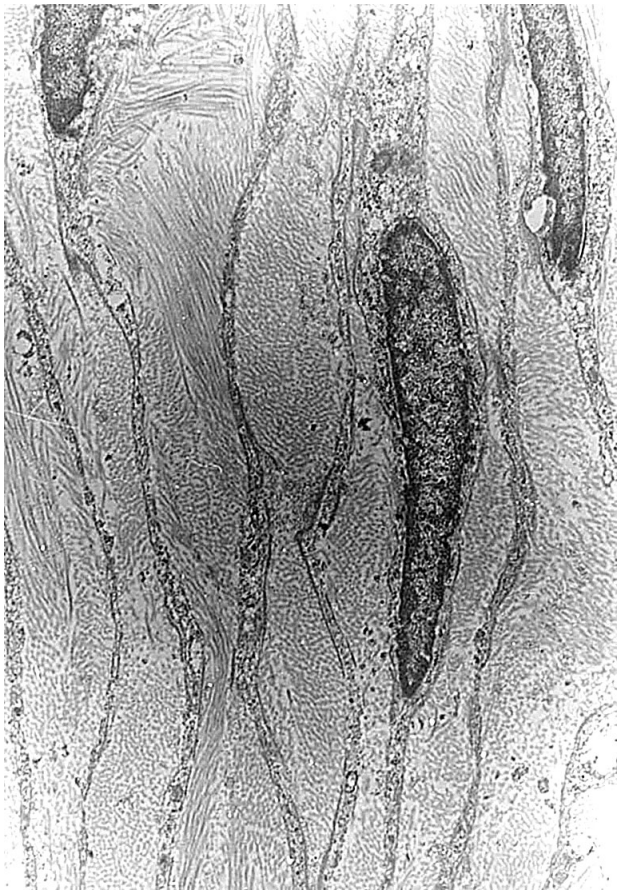

Figure 8. Electron micrograph showing flattened cells with slender, long cytoplasmic processes closely associated with collagen fibrils.

cases were associated with hyperplastic polyps located elsewhere in the colon.[1,2] Adenomas were present in two of our patients and in five previously reported cases.[1] Other associated findings were diverticulosis (two cases), internal haemorrhoids and a prolapsing mucosal polyp (one case each).[1,2] Judging from the clinical and pathological features of the cases we describe and those reported previously, FP of the colon appears to be an entirely benign lesion.

Histologically, our cases resembled those reported by Eslami-Varzaneh *et al.*[1] Yet, our study allowed the identification of previously unrecognized features of this lesion. Masson trichrome stain, performed in six of our cases, allowed the detection of thin, delicate collagen fibres among the tumour cells. We also noted a tendency to zonation in five of our cases with bundles of spindle cells arranged parallel to the surface changing to deeper, haphazardly orientated sheets of plump cells with a focal periglandular or perivascular concentric arrangement. An additional frequent finding was the presence of a thin layer of lamina propria interposed between the surface epithelium and the fibroblastic cells. This feature has been unnoticed previously but it can be observed in Figures 1B and 2B,D from an earlier report.[1] One of our cases deviated from the usual histological picture as it exhibited round whorls of cells that resembled meningothelial-like nodules morphologically similar to those described in the lungs.[3] However, the immunohistochemical results ruled out a meningothelial cell origin.

Perhaps the most striking finding of this study was the presence of hyperplastic (serrated) crypts in the vast majority (80%) of cases of FP. Eslami-Varzaneh *et al.*[1] reported a hyperplastic polyp in three (21%) of their 14 cases immediately adjacent to or admixed with the fibroblastic cells. Likewise, in the series of Zamecnik and Chlumska,[2] one case was a mixed hyperplastic/fibroblastic polyp while a second case had a hyperplastic polyp immediately adjacent to a FP. The admixture of hyperplastic polyps with FP may represent a mere coincidence. However, the high frequency of mixed polyps in this series and the intimate association between the fibroblastic and the epithelial cells support the view that FP with serrated crypts (or mixed fibroblastic/hyperplastic polyp) represents a distinct and frequent variant of this entity. We believe that FP with serrated glands are not particularly uncommon and are being reported either as hyperplastic polyps or hyperplastic polyps with stromal fibrosis for lack of a better term. In fact, FP shares with hyperplastic polyps additional features: both lesions are typically found in the rectosigmoid of adult patients and their size rarely exceeds 5 mm in diameter. In addition, hyperplastic polyps are found in 50% of patients with FP. It can be speculated that a common stimulus is responsible for the development of both types of polyps and/or that a possible epithelial–mesenchymal interaction leads to the development of mixed polyps. Clearly, further research is needed to determine the precise aetiology and pathogenesis of this lesion.

Our findings confirm that the stromal component of FP displays a fibroblastic phenotype. This is based on the histological and ultrastructural appearance of the tumour cells and is further supported by the finding that they express vimentin only and lack reactivity for markers of specific differentiation. Zamecnik and Chlumska[2] evaluated markers of dendritic cells in four FP and found occasional CD34 and consistent fascin reactivity. They suggested that FP might be related to inflammatory fibroid polyp (IFP), a lesion proposed as originating from dendritic cells,[4] since both display a perivascular concentric arrangement of spindle cells, scattered eosinophils and reactivity for CD34 and fascin. However, the perivascular concentric

arrangement of fibroblastic cells and the eosinophilia represent non-specific findings.[5] In addition, CD34 is consistently positive in IFP, whereas it is only rarely and focally expressed in FP.[1] Fascin, proposed as a potential marker of dendritic cell neoplasms,[6,7] has been shown to be positive in IFP.[4] However, Grogg *et al.*[8] reported fascin positivity in a large variety of soft tissue tumours and concluded that fascin does not provide evidence of dendritic cell lineage.

Entities that may be considered in the differential diagnosis of FP include colorectal mucosal spindle cell lesions such as neural lesions, leiomyomas, smooth muscle hamartomas and prolapse-related changes. Neural lesions, mostly ganglioneuromas, may present as small mucosal polyps composed of a mucosal spindle cell proliferation. However, unlike FP they are characterized by the presence of ganglion cells and are typically immunoreactive for S100 protein.[9] Leiomyomas and smooth muscle mucosal hamartomas, a rare lesion mostly seen in patients with tuberous sclerosis, differ from FP in that they are composed of intersecting fascicles of cells with abundant deep eosinophilic cytoplasm and cigar-shaped nuclei, and are immunoreactive for smooth cell markers.[10–12] Mucosal prolapse syndromes, such as solitary rectal ulcer syndrome and inflammatory cloacogenic polyp, are typically found in patients with constipation and other difficulties in defaecation. These lesions may resemble FP as they are composed of hyperplastic crypts separated by a stromal proliferation in the lamina propria. However, the stromal component is of fibromuscular nature and collagen-rich, the glandular component is more prominent than in FP and the surface is frequently villiform, eroded and covered by exudates.[13,14]

In summary, this study validates previous findings on FP, provides additional information about its histological features, and demonstrates that FP with serrated crypts represents a frequent variant of this lesion. We conclude that colonic FP constitutes a distinctive clinicopathological entity characterized by its distal colorectal location, small size, frequent association with hyperplastic polyps, distinct morphological appearance and typical immunonegativity for markers of specific differentiation. Wider recognition of this entity will allow its better characterization and discrimination from other types of colorectal polyps.

Acknowledgements

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Addendum

During the publication of this paper, four additional cases of fibroblastic polyp of the colon were reported (Kalof AN, Pritt B, Cooper K, Hyman NH, Blaszyk H. Benign fibroblastic polyp of the colorectum. *J. Clin. Gastroenterol.* 2005; **39**; 778–781).

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